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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/673,647

09/30/2003

A. Robin Poole

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05/05/2006

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EXAMINER

EWOLDT, GERALD R

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/673,647

Applicant(s)

POOLE, A. ROBIN

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-51 is/are pending in the application.
- 4a) Of the above claim(s) 29-51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply, Sequence</u> . |

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DETAILED ACTION

1. Applicant's election with traverse of Group I in the paper filed 2/13/06, is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election with traverse of the disease species rheumatoid arthritis (RA), is also acknowledged. Upon reconsideration the disease species election requirement has been withdrawn.

2. Claims 29-51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-28 are being acted upon.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. 131 and 132. Specifically, the sequences in the specification, e.g., page 6, must be identified by SEQ ID NOS:.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) Claim 4 recites "ratio" twice in line 3.

B) The claims are vague and indefinite in the recitation of conflicting and opposite conclusions to be drawn from the same comparisons. For example, Claim 1 recites that greater joint destruction is indicated for other types of arthritis when

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C1,C2/C2C ratios increase. Claim 15 recites the opposite, i.e., that greater joint destruction is indicated for other types of arthritis when C1,C2/C2C ratios decrease.

C) The preambles of the claims do not match the conclusions. For example, Claim 1 recites a method of predicting the progression of osteoarthritis (OA), but the comparison of the claim results in a prediction of joint destruction. Claim 8 recites a method of monitoring OA, RA, or other types of arthritis, but the comparison of the claim again results in a prediction of joint destruction. Likewise, Claims 15, 20, 22, and 27 recite methods wherein the preamble of the claims does not match the conclusions drawn.

D) Claims 8 and 22 are nonsensical in the recitation that "an increase or change in" the aforementioned ratios indicates an increase in the progression of joint destruction. Said "change" would also encompass decreases.

6. Claims 13 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step indicating what the determination of the C1,C2/C2C or C2C/C1,C2 ratio indicates. The claims simply recite that a change indicates a change.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the method of the instant claims would function as claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the

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claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

A review of the specification discloses that the method of the instant claims presumably functions through a measurement of C1,C2/C2C or C2C/C1,C2 ratios, wherein a higher C1,C2/C2C indicates the progression of OA and a lower C1,C2/C2C ratio indicates the progression of RA. Additional claims recite the measurement of said ratios as a measure of the monitoring the efficacy of treatment or for identifying agents for treatment. Two brief examples are offered in support of the claimed method.

First note that the specification itself discloses that the claimed method cannot function as broadly claimed. See for example page 9 wherein it is disclosed that the method works only in OA patients "without evidence of generalized OA". See also the example at page 10, wherein it is disclosed that the claimed method does not function in RA patients with "early disease presentation". For these reasons alone the claimed method must be considered to be unpredictable and requiring of undue experimentation. A further review of the examples shows

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that their disclosures must be further questioned. Note that neither example actually discloses any data. Only conclusions are reported. Absent the data used to establish the reported conclusions, the value of said results cannot be established. Also note that in Example 1, "Knees with the highest grade at baseline were excluded". The selective choosing of data points for inclusion in results is not generally considered to result in scientifically credible conclusions.

A review of the relevant art shows that in contrast to what the claims might predict, an increase in C2C is generally considered to indicate the progression of OA. See, for example, Poole (2003, IDS). At page 811 the reference teaches that an increase in C2C accompanies the induction of OA. See also Chu et al. (2002), Figure 1, which teaches similar findings. Regarding RA, see Verstappen et al. (2006), page 5, column 2, wherein it is taught that RA progression is accompanied by increases in both C2C and C1,C2. Also note that Poole (2003) teaches that a number of considerations "confound" the use of biomarkers for the measure of arthritis. Said marker considerations include biomarker concentrations, which vary from tissue to joint, to serum, biomarker half-life, patient age and sex, and even circadian rhythms; none of these considerations are disclosed in the instant specification.

Finally note that the specification discloses nothing regarding the "other types of arthritis" of the claims, yet wherein some claims recite a correlation of disease progression with *increased* C2C/C1,C2, other claims recite a correlation of disease progression with *decreased* C2C/C1,C2. Clearly, both situations, if true, indicate the unpredictability of the claimed method. Accordingly, the method of the instant claims must be considered unpredictable and requiring of undue experimentation.

9. No claim is allowed.


10. Note that a number of references have been lined through on the multiple Form 1449's and have not been considered. Said references are either duplicates, not submitted in the proper format, i.e., author, source, date, etc., or not submitted in their entireties. See MPEP 609.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr.

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Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

12. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


5/6/00
G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: _____

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE